Feature Article

Environmental risks and challenges associated with neonicotinoid insecticides

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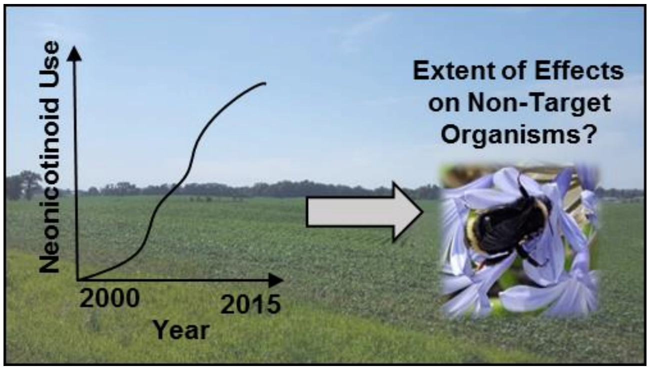

ABSTRACT

Neonicotinoid use worldwide has increased rapidly in recent years with a shift towards insecticide applications as seed coatings rather than aerial spraying. While the use of seed coatings can lessen the amount of overspray and drift, the near universal and prophylactic use of neonicotinoid seed coatings on major agricultural crops has led to widespread detections in the environment (pollen, soil, water, honey). Pollinators and aquatic insects appear to be especially susceptible to the effects of neonicotinoids with current research suggesting that chronic sub-lethal effects are more prevalent than acute toxicity. Meanwhile, evidence of clear and consistent yield benefits from the use of neonicotinoids remains elusive for most crops. Future decisions on neonicotinoid use will benefit from weighing crop yield benefits versus environmental impacts to non-target organisms, and also consider whether there are more environmentally benign alternatives.

BACKGROUND ON NEONICOTINOIDS

Neonicotinoid insecticides have been in use for over two decades. The first neonicotinoid, imidacloprid, was registered for use in 1991. From 1995 to 2002 more neonicotinoids were introduced to the market: nitenpyram and acetamiprid in 1995, thiamethoxam in 1998, thiacloprid and clothianidin in 2001, and dinotefuran in 2002.[1] In the mid-2000s, neonicotinoid use increased rapidly due to changes in application techniques through the increased use of coated seeds and with increasing insect resistance and/or concern over the high mammalian toxicity of other insecticides previously used such as the organophosphates (*e.g.*, chlorpyrifos), carbamates (*e.g.*, carbaryl), and pyrethroids (*e.g*,. bifenthrin).[2,3,4] Neonicotinoid use has continued to increase both in the United States[5] and worldwide.[3,6] Currently, neonicotinoids are the most widely used insecticides in the world representing 25% of the global insecticide market.[1]

Neonicotinoids are synthetic compounds similar in structure to nicotine (Figure 1). They have a common mode of action that affects the central nervous system of insects (binding to nicotinic acetylcholine receptors) making them active against a broad spectrum of insects. They are also systemic insecticides,[6] which means they can be taken up through the roots of plants and translocated to their leaves, flowers, and pollen, making them ideal candidates for seed coatings. Seed coatings in this instance refer to the application of chemical products to the seed prior to sowing to suppress, control, or repel insects and other pests such as fungi that attack seeds, seedlings, or plants.[7] Seed coatings are used for a variety of crops including maize (corn), soybeans, sunflowers, oilseed rape (canola), and cotton.

In addition to their use as seed coatings, neonicotinoids are also applied in agricultural areas as foliar sprays, in-furrow treatments (*e.g.*, soil drenches), and granules. However, neonicotinoid use is not restricted to the agricultural environment. In urban or forested areas, neonicotinoids are applied as tree soil drenches or injections (*e.g.*, for the control of emerald ash borer and hemlock wooly adelgid[8]). Plants grown in garden centers and nurseries are often protected via neonicotinoid foliar sprays, drenches, and/or granular applications.[9,10] Imidacloprid also has a variety of other home uses including lawn and garden applications, and topical flea medicines.[3]

ENVIRONMENTAL FATE

Neonicotinoids are highly soluble in water (log K_{ow} 0.55 to 1.26; log K_{oc} 1.4 to 2.3), somewhat persistent in water and soils (aqueous dissipation half-lives of 4.7 to 40.3 days; soil degradation half-lives of 3 to >1,000 days) and not volatile (<0.002 mPa at 25 °C), making them available for transport away from the area of initial application to different environmental compartments.[11,12,13]

As many neonicotinoids are used as seed coatings they are likely to be found in the crops grown from treated seeds including the leaves, pollen, and nectar. It is estimated that 2 to 20% of the neonicotinoid coating is absorbed by the crop[14,15] and the amount of neonicotinoids in the leaves or pollen can vary. Neonicotinoids have also been detected in wildflowers adjacent to agricultural areas,[16,17] indicating their potential to move away from the point of application area and to be taken up by other non-target plants.

With only a small portion (on average 5%) of the neonicotinoid coating being absorbed by the crop this leaves ~95% of the active ingredient available in the soil and soil water or lost as dust during planting. The amount of seed coating lost as dust during planting can vary though it is a relatively low percentage of the total mass (< 2%).[18] Seed coating loss varies according to drilling method and is affected by the use of lubricants during planting which have been optimized in recent years to reduce dust emissions.[19]

Neonicotinoids have been measured in the soil of fields planted with seeds treated for a variety of crops. Concentrations in the soil increase in subsequent years after repeated use[11,20] though concentrations have been found to plateau after approximately 4 to 6 years of treated seed use.[21,22] It has also been noted that after the cessation of treated seeds, neonicotinoids can still be detected several years later.[20,23]

As highly water soluble compounds, neonicotinoids have been frequently detected in waterways around the world including surface water runoff (rivers, streams),[21,24,25,26,27] groundwater,[28,29,30] and wetlands.[31,32] Imidacloprid, the first commercially available neonicotinoid, was detected in 89 to 100% of water samples collected during monitoring studies of global surface waters.[24,25,27,28] Studies that measured multiple neonicotinoids in the US detected at least one neonicotinoid in 76% of samples from an intensely agricultural area within the Midwestern US,[26] with peak concentrations occurring shortly after planting, and in 53% of samples that included a variety of land uses.[33] In the Canadian Prairies, neonicotinoids were frequently detected in wetlands during (post-seeding: 62%) and outside (pre-seeding: 91%) of the growing season;[32] additionally, in these areas snowmelt is a major source of neonicotinoid contamination with wetlands likely to be contaminated before seeding has occurred.[34] The source of neonicotinoids in water can vary from overspray to particulates[19] to runoff from seed coatings[26,30] or soil applications.[29] In general, agricultural areas have frequent detections of the three neonicotinoids used primarily as seed coatings (*i.e.*, clothianidin, imidacloprid, and thiamethoxam), while urban areas have frequent detections of imidacloprid.[33]

EFFECTS ON NON-TARGET ORGANISMS

Neonicotinoids affect the central nervous system of insects, and do not discriminate between target (*e.g.*, corn rootworm, flea beetle) and non-target insects (*e.g.*, bees). An important mechanism of neurotoxicity for neonicotinoids is the almost irreversible binding to nicotinic acetylcholine receptors in insects[35] making low-level continual exposures to neonicotinoids likely to lead to cumulative effects.[36] Non-target organisms expected to be exposed to neonicotinoids at levels of concern include pollinators, aquatic insects, and birds.

Pollinators. Concern over the environmental impacts of neonicotinoids began in 1996 when French beekeepers linked the use of imidacloprid, at the time a new product, with honeybee (*Apis mellifera*) hive deaths.[20] Honeybees have remained at the center of concerns over neonicotinoid use ever since; a search of Web of Science™ (Clarivate Analytics, 2017) with the terms "neonicotinoid" and "*Apis*" reveals 333 papers on the topic, with more than half of them published since 2015.

The three most commonly detected neonicotinoids (clothianidin, imidacloprid and thiamethoxam) are classified as being highly toxic to bees (acute toxicity values, LD_{50}, from oral ingestion are 1 to 5 ng/bee).[37] Being systemic within the crop, pollinators can be exposed to neonicotinoids when they consume the nectar or pollen of a treated crop that flowers[11] and pollinators can also be exposed through the dust from seed coatings.[38] Additionally, neonicotinoids frequently contaminate the pollen and nectar of wildflowers growing in the vicinity of treated crops, increasing the likely duration and extent of pollinator exposure to neonicotinoids.[39,40,41,42] Screening the nectar and pollen stores within honeybee or bumblebee nests reveals that neonicotinoids are often present.[12,41,43,44] For example, a recent study of honey samples collected from around the world found neonicotinoids in 75% of samples, with 45% of samples containing multiple neonicotinoids.[45] Typically, concentrations of neonicotinoids in honey and pollen collected by bees are in the range 1 to 10 ng/g, occasionally much higher, and approximately corresponding to concentrations found in pollen and nectar of crops and wildflowers.[12]

Much less is known about exposure of other pollinators (*e.g.*, wild bees, butterflies, flies) to neonicotinoids, but dietary exposure is likely to be similar to that of honeybees. Analysis of the pesticides in composite samples of wild (non-honey) bees caught in traps in Colorado, USA found at least one neonicotinoid in 48% of the samples with mean concentrations of 6.5 to 26 ng/g;[46] of course bees that had received a lethal dose would be unlikely to fly into traps, so these measures are likely to be underestimates. Overall, it is clear that pollinators are routinely and chronically exposed to one or more neonicotinoids.

There is now considerable evidence that these levels of exposure are sufficient to have deleterious effects on bees. In laboratory and semi-field studies, exposure to field realistic doses has been shown to impair learning and the accuracy of navigation, decrease foraging success, suppress the immune response, reduce the viability of sperm stores in queens, reduce queen longevity, reduce growth of bumblebee colonies and reduce the number of new queens they produce.[47,48,49,50,51] Full field trials are hard to perform with free-flying bees, particularly given the challenge of finding control areas without neonicotinoids. Nonetheless, some large field trials have been performed.[41] In Sweden,[52] researchers found that bumblebee colonies placed next to oilseed rape fields treated with clothianidin performed markedly more poorly than controls; solitary mason bees (*Osmia bicornis*) failed to breed entirely when adjacent to treated fields, but honeybee hives showed no measureable effects. Similar results were reported for a very large field trial conducted across the United Kingdom, Germany and Hungary, with clear adverse effects on bumblebees and mason bees (*Osmia*) and variable impacts on honeybees.[53] It should be noted that some field trials have found no negative impacts,[54] and it seems that honeybee colonies may be less susceptible to neonicotinoids than are wild bees, perhaps because their relatively large size colony buffers them against impacts.[44]

Have the various effects of neonicotinoids reported from laboratory, semi-field, and some field trials resulted in measureable real-world impacts on populations of bees or other non-target insects? Budge et al.[55] found that geographic and temporal patterns of imidacloprid use predicted the frequency of honeybee colony losses in the UK. A subsequent analysis of population change in wild bees in England found that declines were predicted by regional patterns of neonicotinoid use.[56] Similar patterns have since been revealed for butterflies in the UK and California, USA.[57,58] Overall, there is now a substantial body of evidence suggesting that neonicotinoids are contributing to health issues being experienced by domestic honeybees, and to declines of wild bees and butterflies.

Aquatic insects. Beyond pollinators, neonicotinoids are known to negatively impact aquatic ecosystems, especially non-target aquatic invertebrate communities. The potential for neonicotinoid toxicity (acute and/or chronic) toward aquatic arthropods varies greatly. Insects are typically the most sensitive,[59] but much of these data are derived from single-species laboratory toxicity studies and/or controlled experiments. A review of 214 acute and chronic toxicity tests indicate that the orders Ephemeroptera (mayflies), Trichoptera (caddisflies), and Diptera (flies including Chironomid midges) were consistently the most sensitive taxa to neonicotinoids.[59] Although direct toxicity of neonicotinoids is a concern, within aquatic insects, several sub-lethal endpoints including behavior, reproduction, immobility, feeding inhibition, and delayed emergence are all shown to be impacted by neonicotinoids.[60,61,62,63] Sub-lethal responses by individual insect species often vary; however, impacts on multi-species communities, ecosystem processes, species interactions, and functions have also been observed.

Elevated surface water concentrations of imidacloprid in the Netherlands in the range from hundreds of ng/L up to 200,000 ng/L have been correlated with direct effects on invertebrates.[25] At field-realistic concentrations of <1,000 ng/L, shifts in predatory-prey interactions, reduced leaf consumption, and increased carnivorous behavior have been observed in experimental settings.[65,66] Additional environmental variables and other stressors including temperature, food limitation, seasonality, and also life-history stage all likely influence sensitivity toward neonicotinoids.[67] Compared to laboratory studies, chronic studies (>28 days), experimental mesocosms,[51] and field-validated studies assessing neonicotinoid impacts on aquatic invertebrates remain limited. More extensive testing of neonicotinoids on standard test species exist (*e.g.*, *Daphnia magna*); however, these test species are 100,000 times less sensitive to neonicotinoids than species such as caddisflies, midges, and mayflies, which support aquatic and terrestrial food webs.[59] In spite of numerous studies indicating that many individual aquatic invertebrates are sensitive to neonicotinoids, much of the literature is based on evaluations of imidacloprid[51,59] where comparative data on other neonicotinoids remains limited.

Because of the differences in species sensitivity, aquatic benchmarks vary by the risk assessment/level of protectiveness (Table 1 shows values from the United States,[68] Canada,[69] and the European Union[70]). The current US Environmental Protection Agency (USEPA) aquatic life benchmarks for imidacloprid acute and chronic toxicity are 385 and 10 ng/L, respectively.[68] The current USEPA values are similar to those reported by Morrissey et al. [59] who found that in global surface water studies the thresholds of 200 and 35 ng/L (for acute and chronic toxicity, respectively) were exceeded in 81% of the studies reporting maximum concentrations and 74% of the studies reporting average concentrations.

Birds. Granivorous birds can consume neonicotinoid-coated seeds during planting causing lethal or sub-lethal direct effects;[71,72] sub-lethal effects can include a loss of body mass or impaired flying orientation which is critical for maintaining the correct migratory direction.[72]

Even the ingestion of an individual coated seed can be toxic or have an effect on a bird's reproductive ability;[73] yet, birds may avoid these coated seeds if other food is available.[74] Birds are likely to experience indirect effects from neonicotinoids, especially for insectivorous birds where their food source can be depleted by the use of neonicotinoids.[75] In North America, Prairie Pothole Region wetlands are critical staging areas for breeding birds (*e.g.*, aerial insectivores, waterfowl, water birds) and produce the majority of food resources for wetland dependent organisms. Many of these wetlands are contaminated on an annual basis,[32,76] yet it is unclear whether neonicotinoids have in turn impacted aquatic-terrestrial linkages or food webs across this region.

CHEMICAL MIXTURES.

In addition to the above concerns about individual neonicotinoid toxicity, there is also little known about the potential toxicity of multiple neonicotinoids that are often detected together, or the toxicity of their metabolites/environmental degradates that may also be present. In aquatic organisms, neonicotinoid mixtures have combined effects that cannot be predicted by simple additivity.[77] Previous studies have shown neonicotinoid metabolites to be as toxic as the parent compound[78,79] so degradation may not confer reduced toxicity. Neonicotinoids occur in a complex mixture of multiple environmental stressors. Seed coatings not only include neonicotinoid insecticides but may also contain multiple fungicides, herbicide safeners, nematicides, and plant growth regulators along with surfactants/adjuvants.[7] In the environment, neonicotinoids can co-occur with other contaminants such as fertilizers, metals and pharmaceuticals. These multiple stressors can act additively, as synergists, or as antagonists; evaluating the effects of chronic exposure of non-target organisms to complex and changing mixtures of chemicals poses a major challenge to scientists.

CURRENT USE PATTERNS AND EVALUATIONS

Currently, nearly 100% of maize planted in the US and canola planted in Canada have a seed coating that includes a neonicotinoid, and these seed coatings are also used in many other crops (soybeans, oilseed rape, cereals, rice, cotton, sunflowers),[7] increasing the use of neonicotinoids worldwide. The benefits of seed coatings depend on the type of crop; some crops have seen an increase in yields with coated seeds while others have not. Publications on the benefits of seed treatments to specific crops are not commonly found in peer-reviewed literature.[80] For soybeans, one study found an increase in average yield in a 2013 survey[81] while a USEPA study[82] using data from 2008 to 2012 found seed treatments provide negligible benefits. There have been no increase in the yields of sunflowers.[83] In rice, there was an increase in yields in areas of moderate and high pest pressures but these were not always economical.[84] In Europe, yields of oilseed rape, sunflower, and maize have remained at or above previous levels following the banning of use of neonicotinoids on these crops in 2013.[85, 86]

The timing of the seed coatings protection, occurring in the early growing season (typically spring) may not coincide with pest pressures (often highest in summer). One study[15] found that clothianidin may provide protection against early season pests but overall translocation into maize is small (<2%) indicating that only small percentage of the seed coating is available to confer insecticidal activity in the plant. Seed coatings as currently used are violating key principals of integrated pest management because the prophylactic neonicotinoid seed treatments are targeting “occasional pests”[80] and there is evidence that pest resistance is increasing with increasing neonicotinoid use.[1] The prophylactic use of neonicotinoids may make them less effective towards target pests in the future which could be of concern to growers if sufficient replacement insecticides do not exist.

Seed coatings are one of many tools used as "precision agriculture," in this case the mode of application is intended to reduce the exposure of the insecticides to humans and the environment while still providing protection against insects. Theoretically, seed treatments can lessen the impact on the environment compared to previous spray applications. In the case of neonicotinoids this assumes that most of the coating is absorbed by the crop, which, as discussed above, is not typical. Additionally, the prophylactic use of neonicotinoids and their routine application to a growing number of crops in many regions means that overall insecticide use has increased. In Canada, there was ~30% increase in the amount of crop land treated with neonicotinoids from 2009-2012;[32] however, these estimates are likely conservative. In the US, prior to the use of neonicotinoid treated seeds only about 35% of maize acres received insecticide applications versus the current near 100% application of neonicotinoids.[80] In surface water samples, neonicotinoids have been found more frequently and in higher concentrations than historically used organophosphate and carbamate insecticides in previous investigations of similar landuse areas.[26]

With an increase in concern over potential environmental effects of neonicotinoids they are currently under scrutiny across the globe. In 2013, the European Union banned the use of three neonicotinoids (clothianidin, imidacloprid, thiamethoxam) for any use on crops attractive to bees (EU, 2013).[87] The USEPA is reevaluating the registration of neonicotinoids, especially in relation to pollinators.[88] In Ontario, Canada, the goal is to cut acres planted with neonicotinoid-treated maize and soybean seed by 80% by 2017.[89]

FUTURE CONSIDERATIONS FOR NEONICOTINOIDS

There is a rapidly growing body of scientific evidence to help decision makers weigh the benefits of neonicotinoid use against adverse effects on non-target organisms, but many knowledge gaps remain. Future research should focus on:

- Evaluating the cost-effectiveness of neonicotinoid use. Prophylactic use as seed coatings should be reserved for crops and situations where it produces a yield benefit and where other alternatives are lacking. Judicious rather than blanket use of neonicotinoids would limit pest resistance and reduce environmental impacts.
- Where neonicotinoids appear to be the best available option, effective methods are needed to mitigate impacts, such as minimizing planter dust and spillage of seeds, reducing surface runoff, and exploring the potential of using riparian vegetation to reduce contamination of aquatic systems.
- Understanding the impacts on non-target organisms of chronic exposure to complex mixtures of multiple neonicotinoids, neonicotinoid metabolites, other agrochemicals and adjuvants, and other environmental pollutants.
- Investigating how best to implement comprehensive integrated pest management systems which ordinarily would not include prophylactic use of any pesticide.

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The authors declare no competing financial interests

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Table 1. Comparison of aquatic benchmarks for imidacloprid.

Source		Value (ng/L)
USEPA Aquatic Life Benchmark – Invertebrates[66]	acute	385
	chronic	10
Canadian Council of Ministers of the Environment Water Quality Guideline[67]		230
European Water Framework Directive[68]	acute	200
	chronic	8.3

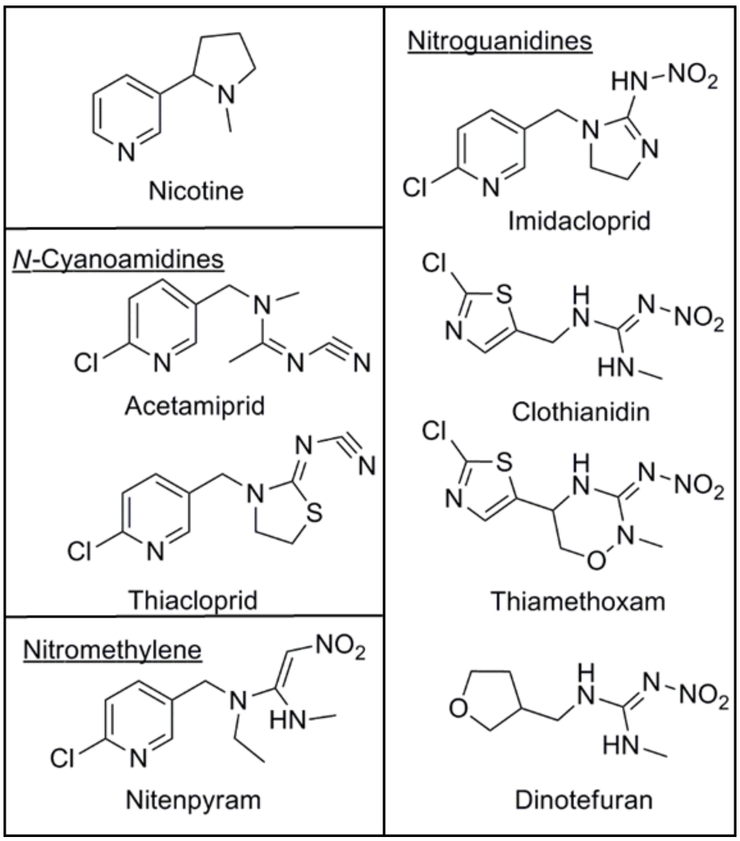

Figure 1. Structures of nicotine and the synthetic neonicotinoid insecticides.

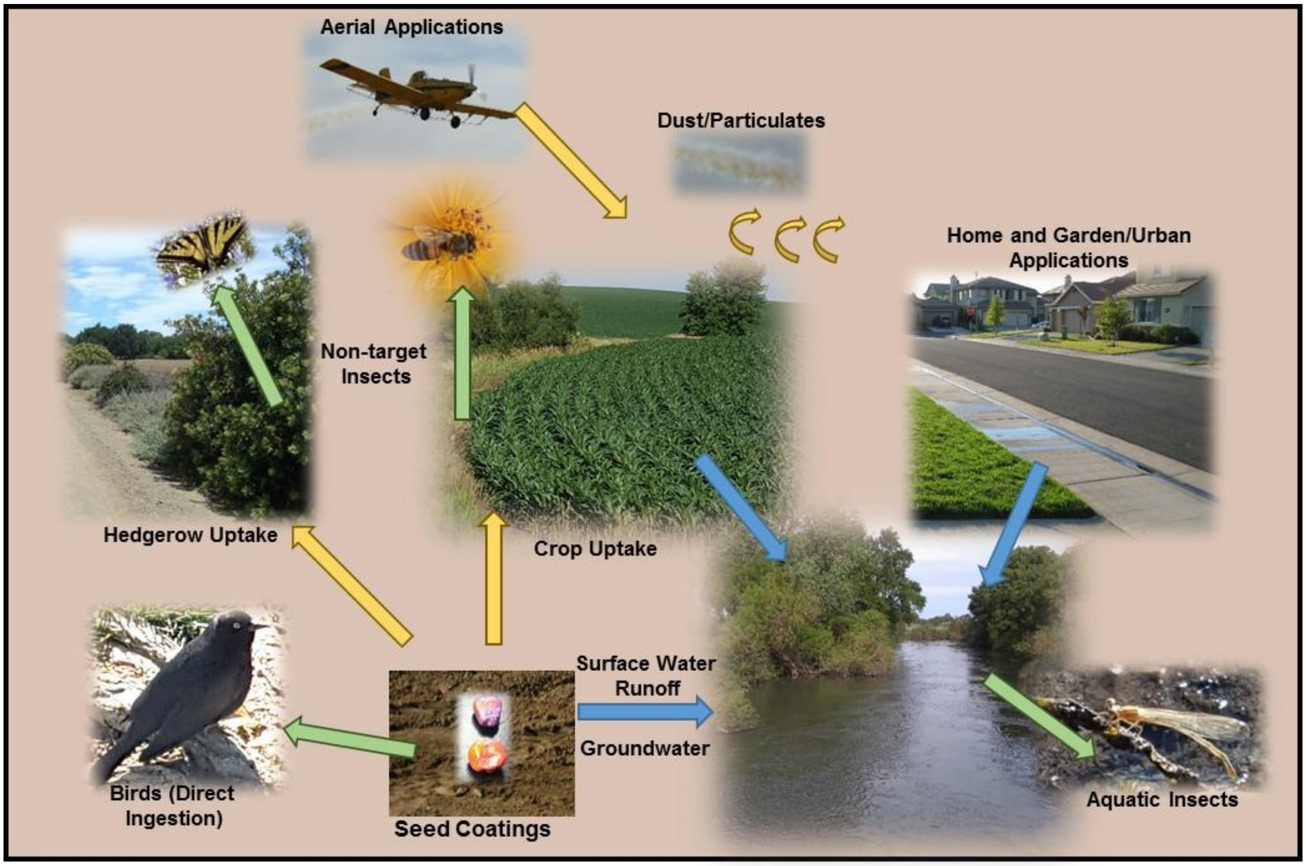

Figure 2. Routes of possible neonicotinoid transport and exposure in the environment.